Access DB# 81868

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: GARY Counts Examiner #: 78696 Date: 12-9-02
Art Unit: 1641 Phone Number 30 5-1444 Serial Number: 09/844815
Mail Box and Bldg/Room Location: 7D16 Results Format Preferred (circle): PAPER DISK E-MAIL
7E12

If more than one search is submitted, please prioritize searches in order of need. mpj

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Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Urinary trypsin inhibitor ASSAY containing a chelating Agent.

Inventors (please provide full names): Gary Rehm, Michael Pugia, Paul Carey

Earliest Priority Filing Date: 05-15-2000

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Please search Attached Claim 1.

* See Attached claim 7 for specific chelating agents (~~the acid~~).

Mary Jane Ruhl
Tech. Info. Specialist, STIC
TC-1600
CM-1, Room 6A-06
Phone: 605-1155

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STAFF USE ONLY

Searcher: Ruhl
Searcher Phone #:
Searcher Location:
Date Searcher Picked Up: 12/11/02
Date Completed: 12/16/02
Searcher Prep & Review Time:
Clerical Prep Time:
Online Time:

Type of Search

NA Sequence (#)
AA Sequence (#)
Structure (#)
Bibliographic
Litigation
Fulltext
Patent Family
Other

Vendors and cost where applicable

STN
Dialog
Questel/Orbit
Dr.Link
Lexis/Nexis
Sequence Systems
WWW/Internet
Other (specify)

PTO-1590 (8-01)

1. An assay for trypsin inhibitors in urine which comprises (a) contacting a urine test sample with a buffered assay medium consisting essentially of (i) trypsin, (ii) a substrate for trypsin which will produce a detectable response when cleaved by trypsin and (iii) a polycarboxylic chelating agent in sufficient quantity to inhibit interference with the assay from calcium present in the urine as assay reagents, wherein calcium present in the buffered assay medium is not present in sufficient quantity to interfere with the binding of calcium present in the urine test sample with the polycarboxylic chelating agent, and (b) correlating the concentration of trypsin inhibitor with the detectable response from the cleaving of the substrate.

6. The assay of Claim 5 wherein the assay reagents are impregnated into a dry test device of a material through which the urine test sample can flow by dipping the dry test device into the buffered assay medium with subsequent drying of the solvent.

7. The assay of Claim 1 wherein the chelating agent is ethylene glycol bis (β-aminoethyl ether) N,N,N',N'-tetraacetic acid (EGTA); ethylenediaminetrata acetic acid (EDTA); iminodiacetic acid (IDA); nitrilotriacetic acid (NTA); diethylenetriaminipentaacetic acid (DTPA); triethylenetriamine-hexa-acetic acid (TTHA); 2,3-propylenediamino-tetra-acetic acid (UEDTA) and 1,2-diaminocyclohexanetetra-acetic acid.

8. The assay of Claim 1 wherein the trypsin is present in an amount of from 10 to 750 IU/mL, the chelating agent is present in an amount of from 0.2 to 50 mM, the trypsin substrate is present in a concentration of from 0.2 to 50 mM and the pH is buffered at a level of from 6.0 to 8.0.

9. The assay of Claim 8 wherein the trypsin concentration is from 100 to 500 IU/mL, the chelating agent is present in a concentration of from 10 to 25 mM, and the pH is at a level of from 7.0 to 8.0.

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=> d his full

     (FILE 'HOME' ENTERED AT 16:54:06 ON 13 DEC 2002)

     FILE 'REGISTRY' ENTERED AT 16:54:25 ON 13 DEC 2002
                E EGTA/CN
L1              1 SEA ABB=ON  EGTA/CN
                E EDTA/CN
L2              1 SEA ABB=ON  EDTA/CN
                E NITRILOTRIACETIC ACID/CN
L3              1 SEA ABB=ON  "NITRILOTRIACETIC ACID"/CN
                E IMINODIACETIC ACID/CN
L4              1 SEA ABB=ON  "IMINODIACETIC ACID"/CN
                E DIETHYLENETRIAMINIPENTAACETIC ACID/CN
                E DTPA
                E DTPA/CN
L5              1 SEA ABB=ON  DTPA/CN
                E TTHA/CN
L6              1 SEA ABB=ON  TTHA/CN
                E UEDTA/CN
                E PROPYLENEDIANINOTETRAACETIC ACID/CN
                E PROPYLENEDIAMINOTETRAACETIC ACID/CN
L7              1 SEA ABB=ON  "PROPYLENEDIAMINETETRAACETIC ACID"/CN
                E 2,3-PROPYLENEDIAMINOTETRAACETIC ACID/CN
                E 2,3-PROPYLENEDIAMINETETRAACETIC ACID/CN
                E PROPYLENEDIAMINOTETRAACETIC ACID/CN
                E 1,2-DIAMINOCYCLOHEXANETETRAACETIC ACID/CN
L8              1 SEA ABB=ON  "1,2-DIAMINOCYCLOHEXANETETRAACETIC ACID"/CN
L9              8 SEA ABB=ON  L1 OR L2 OR L3 OR L4 OR L5 OR L6 OR L7 OR L8

     FILE 'HCAPLUS' ENTERED AT 17:01:35 ON 13 DEC 2002

L10        101593 SEA ABB=ON  L9 OR ?EGTA? OR ?EDTA? OR ?DTPA? OR ?TTHA?
L11          7995 SEA ABB=ON  (?IMINODIACETIC? OR ?IMINO?(W)?DIACETIC? OR
                  ?NITRILOTRIACETIC? OR ?NITRILO(W)TRIACETIC? OR ?PROPYLENEDIAMIN
                  OTETRAACETIC? OR ?PROPYLENEDIAMINO(W)TETRA(W)ACETIC? OR
                  ?DIAMINOCYCLOHEXANETETRAACETIC? OR ?DIAMINO(W)CYCLOHEXANE(W)TET
                  RA(W)ACETIC?)(W)?ACID?
L12        104964 SEA ABB=ON  L10 OR L11
L13             8 SEA ABB=ON  L12 AND URINARY(3A)(TRYPSIN OR TRYPSIN(3A)SUBSTRATE
                  )
L14          1838 SEA ABB=ON  L12 AND (TRYPSIN OR TRYPSIN(3A)SUBSTRATE)

     FILE 'HCAPLUS' ENTERED AT 17:46:29 ON 13 DEC 2002

L15            11 SEA ABB=ON  L12 AND URIN?(3A)(?TRYPSIN? OR ?TRYPSIN(3A)SUBSTRAT
                  E?) - results attached

     FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO' ENTERED AT
     17:50:28 ON 13 DEC 2002
L16            17 SEA ABB=ON  L15
L17             9 DUP REMOV L16 (8 DUPLICATES REMOVED) - results attached
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=> d que stat l15
L1             1 SEA FILE=REGISTRY ABB=ON  EGTA/CN
L2             1 SEA FILE=REGISTRY ABB=ON  EDTA/CN
L3             1 SEA FILE=REGISTRY ABB=ON  "NITRILOTRIACETIC ACID"/CN
L4             1 SEA FILE=REGISTRY ABB=ON  "IMINODIACETIC ACID"/CN
L5             1 SEA FILE=REGISTRY ABB=ON  DTPA/CN
L6             1 SEA FILE=REGISTRY ABB=ON  TTHA/CN
L7             1 SEA FILE=REGISTRY ABB=ON  "PROPYLENEDIAMINETETRAACETIC
                 ACID"/CN
L8             1 SEA FILE=REGISTRY ABB=ON  "1,2-DIAMINOCYCLOHEXANETETRAACETIC
                 ACID"/CN
L9             8 SEA FILE=REGISTRY ABB=ON  L1 OR L2 OR L3 OR L4 OR L5 OR L6 OR
                 L7 OR L8
L10       101593 SEA FILE=HCAPLUS ABB=ON  L9 OR ?EGTA? OR ?EDTA? OR ?DTPA? OR
                 ?TTHA?
L11         7995 SEA FILE=HCAPLUS ABB=ON  (?IMINODIACETIC? OR ?IMINO?(W)?DIACETI
                 C? OR ?NITRILOTRIACETIC? OR ?NITRILO(W)TRIACETIC? OR ?PROPYLENE
                 DIAMINOTETRAACETIC? OR ?PROPYLENEDIAMINO(W)TETRA(W)ACETIC? OR
                 ?DIAMINOCYCLOHEXANETETRAACETIC? OR ?DIAMINO(W)CYCLOHEXANE(W)TET
                 RA(W)ACETIC?)(W)?ACID?
L12       104964 SEA FILE=HCAPLUS ABB=ON  L10 OR L11
L15           11 SEA FILE=HCAPLUS ABB=ON  L12 AND URIN?(3A)(?TRYPSIN? OR
                 ?TRYPSIN(3A)SUBSTRATE?)


=> d ibib abs hitrn 1-11 l15

L15  ANSWER 1 OF 11  HCAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:        2001:850805  HCAPLUS
DOCUMENT NUMBER:         135:368535
TITLE:                   Urinary trypsin inhibitor assay
                         containing a polycarboxylic chelating agent
INVENTOR(S):             Rehm, Gary B.; Pugia, Michael J.; Corey, Paul F.
PATENT ASSIGNEE(S):      Bayer Corporation, USA
SOURCE:                  Eur. Pat. Appl., 9 pp.
                         CODEN: EPXXDW
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE          APPLICATION NO.  DATE
     ---------------   ----  --------      ---------------  --------
     EP 1156121         A2   20011121      EP 2001-110137   20010504
          R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
     CA 2334321         AA   20011115      CA 2001-2334321  20010206
     AU 2001026506      A5   20020725      AU 2001-26506    20010313
     US 2001055816      A1   20011227      US 2001-844815   20010430
     NO 2001002262      A    20011116      NO 2001-2262     20010508
     JP 2002014096      A2   20020118      JP 2001-142654   20010514
PRIORITY APPLN. INFO.:                   US 2000-204032P  P  20000515
AB   Disclosed is an assay for detg. the presence and concn. of trypsin
     inhibitor in urine samples.  The assay reagents, which may be
     used either in the liq. or dry states, include trypsin, a trypsin
     substrate and a polycarboxylic chelating agent.  The inclusion of the
     chelating agent in the assay has been found to reduce variation in the
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assay results.
IT **60-00-4, EDTA**, biological studies **67-42-5, EGTA 67-43-6, DTPA 139-13-9, Nitrilotriacetic acid 142-73-4, Iminodiacetic acid 482-54-2**, 1,2-**Diaminocyclohexanetetraacetic acid 869-52-3, TTHA 4408-81-5**
RL: ARG (Analytical reagent use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(chelating agent; **urinary trypsin** inhibitor assay contg. polycarboxylic chelating agent)

L15 ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:626367 HCAPLUS
DOCUMENT NUMBER: 131:239729
TITLE: A method and a kit for assaying **urinary trypsin** inhibitor
INVENTOR(S): Okamoto, Kazuhiro; Fukunaga, Satoshi
PATENT ASSIGNEE(S): Kyoto Daiichi Kagaku Co., Ltd., Japan
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9949076	A1	19990930	WO 1999-JP972	19990226
W: CN, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
JP 11318493	A2	19991124	JP 1999-36909	19990216
JP 3059433	B2	20000704		

PRIORITY APPLN. INFO.: JP 1998-72712 A 19980320
JP 1998-72713 A 19980320

AB An accurate method is described for assaying **urinary trypsin** inhibitor (UTI) by inactivating .alpha.1-antitrypsin (.alpha.1-AT) in a sample, mixing a trypsin soln. with the sample, adding a substrate to initiate an enzyme reaction, and then, measuring a change in absorbance. .alpha.1-AT can be inactivated either by adding a protease other than trypsin to the sample soln. and reacting the protease with .alpha.1-AT to form the complex, or by adding an oxidizing agent to the sample. As a protease to inactivate .alpha.1-AT, elastase or subtilisin can be used. As an oxidizing agent to inactivate .alpha.1-AT, sodium iodate, iodine, copper sulfate or iron trichloride can be used. The amt. of UTI in a urine sample was accurately detd. by this method using subtilisin as an example.
IT **60-00-4, EDTA**, analysis
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(method and kit for assaying **urinary trypsin** inhibitor)
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 11 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:394241 HCAPLUS
DOCUMENT NUMBER: 129:62957

TITLE: Inhibitors of invasive tissue remodelling for use as contraceptives and antitumor agents
INVENTOR(S): Lund, Leif Roge; Dano, Keld; Stephens, Ross; Brunner, Nils; Solberg, Helene; Holst-Hansen, Claus; Nielsen, John Romer
PATENT ASSIGNEE(S): Fonden Til Fremme Af Eksperimentel Cancerforskning, Den.; Dano, Keld; Stephens, Ross; Brunner, Nils; Solberg, Helene; Holst-Hansen, Claus; Nielsen, John Romer
SOURCE: PCT Int. Appl., 113 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9824474	A1	19980611	WO 1997-DK555	19971208
W: AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9851876	A1	19980629	AU 1998-51876	19971208
EP 942746	A1	19990922	EP 1997-946746	19971208
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 2002099004	A1	20020725	US 2001-995636	20011129

PRIORITY APPLN. INFO.:
DK 1996-1402 A 19961206
WO 1997-DK555 W 19971208
US 1999-319464 B1 19990827

AB The invention pertains to novel methods for preventing or arresting invasive remodelling in mammals by utilising a combination of in vivo inhibition of plasmin and in vivo inhibition of certain other proteolytic enzymes, notably metalloproteases. The method can e.g. be used as a novel alternative to current methods of contraception as well as antifungal and antibacterial treatment. The preferred embodiments relate to treatment and prevention of neoplastic diseases by use of these combinations. Further, the invention relates to novel compns. which comprises a plasmin inhibitor in admixt. with an inhibitor of another proteolytic enzyme, preferably an inhibitor of a metalloprotease.

IT **60-00-4**, **Edta**, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors of invasive tissue remodelling for use as contraceptives and antitumor agents)

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 4 OF 11 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:184066 HCAPLUS
DOCUMENT NUMBER: 126:235525

TITLE: Long-term stability of albumin, protein HC, immunoglobulin G, .kappa.- and .lambda.-chain-immunoreactivity, orosomucoid and .alpha.1-**antitrypsin** in **urine** stored at - 20.degree.C
AUTHOR(S): Tencer, Jan; Thysell, Hans; Andersson, Karin; Grubb, Anders
CORPORATE SOURCE: Department of Nephrology, Lund University Hospital, Lund, S-221 85, Swed.
SOURCE: Scandinavian Journal of Urology and Nephrology (1997), 31(1), 67-71
CODEN: SJUNAS; ISSN: 0036-5599
PUBLISHER: Scandinavian University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The stability of albumin, protein HC, IgG, .kappa.- and .lambda.-chain immunoreactivity, orosomucoid and .alpha.1-**antitrypsin** in **urine** stored at - 20.degree.C for up to 24 mo was investigated. Significant decreases of the median concn. values for protein HC, IgG and .alpha.1-antitrypsin were obsd. for native urine. Addn. to urine of a preservative soln. contg. benzamidinium chloride, **EDTA**, tris(hydroxymethyl)-aminomethane and azide prevented the decreases of the concn. values for protein HC and IgG but not for .alpha.1-antitrypsin. The median concn. values for albumin, orosomucoid and .kappa.- and .lambda.-chain immunoreactivity did not change significantly upon storage of native urine, nor for urine with the preservative soln.

IT **60-00-4**, **EDTA**, uses
RL: NUU (Other use, unclassified); USES (Uses)
(long-term stability of albumin, protein HC, IgG, .kappa.- and .lambda.-chain-immunoreactivity, orosomucoid and .alpha.1-**antitrypsin** in **urine** stored at - 20.degree.C)

L15 ANSWER 5 OF 11 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:356239 HCAPLUS
DOCUMENT NUMBER: 122:287553
TITLE: Kunitz-type trypsin inhibitor prevents LPS-induced increase of cytosolic free Ca2+ in human neutrophils and HUVEC cells
AUTHOR(S): Kanayama, Naohiro; Halim, Abdul; Maehara, Kayoko; Kajiwara, Yoyoi; Fujie, Michio; Terao, Toshihiko
CORPORATE SOURCE: Dep. Obstetrics and Gynecology, Hamamatsu Univ. School Medicine, Hamamatsu, 431-31, Japan
SOURCE: Biochemical and Biophysical Research Communications (1995), 207(1), 324-30
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The protease inhibitor part of inter-.alpha. trypsin inhibitor is identical to **urinary trypsin** inhibitor (UTI). Preincubation of neutrophils and HUVEC cells with UTI inhibited increase of cytosolic free Ca2+ induced by LPS. Increase of cytosolic free Ca2+ induced by LPS in the presence of **EGTA** was also inhibited by UTI. In contrast, UTI did not inhibit increase of cytosolic free Ca2+ in cells stimulated by Ca2+ ionophore with or without **EGTA**. The effects of nine synthetic peptides of UTI on the concn. of cytosolic free Ca2+ in the neutrophils induced by LPS were examd. Preincubation with a peptide of UTI domain 2, NLPIVRGPCAFIQL (83-97), was completely inhibited

by the increase of cytosolic free Ca2+ in neutrophils. This region is identical to the trypsin inhibitor site of UTI. We propose that a function of UTI other than as a protease inhibitor is in regulation of intracellular Ca2+ and that this is due to its trypsin inhibitor region.

L15 ANSWER 6 OF 11 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:265365 HCAPLUS
DOCUMENT NUMBER: 122:52571
TITLE: Intrauterine defensive mechanism of amniotic fluid and fetal membranes
AUTHOR(S): Kanayama, Naohiro
CORPORATE SOURCE: Department Obstetrics and Gynecology, Hamamatsu University School Medicine, Hamamatsu, Japan
SOURCE: Nippon Sanka Fujinka Gakkai Zasshi (1994), 46(8), 673-85
CODEN: NISFAY; ISSN: 0300-9165
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB To det. the intrauterine defensive role of **urinary trypsin** inhibitor (UTI), the authors studied the effects of UTI in human amniotic fluid, fetal membranes and myometrium. The level of UTI was 94 U/mL in neonatal urine (compared to 8.0 U/mL in adult urine) and 88 U/mL in amniotic fluid, indicating that the main source of UTI in the amniotic fluid is fetal urine. UTI was concd. in the vernix, fetal intestine, amniotic membranes and uterine myometrium. Term amnion was darkly stained for UTI, whereas in premature deliveries, UTI staining was markedly decreased. In myometrium, the concn. of UTI increased during pregnancy compared to the nonpregnant state. Placentas also stained well for UTI at term. Thus, UTI has an important role in amniotic fluid, fetal membranes, placenta, and myometrium. UTI inhibited neutrophil elastase activity as well as trypsin activity. Its inhibitory activity was increased in the presence of lipid. Lipopolysaccharide (LPS)-stimulated amnion cells trapped more UTI than unstimulated amnion cells. UTI in amnion cells was released after addn. of 1% meconium solns. UTI inhibited the effect of IL-1, TNF, and interleukin-8 on amnion. These results indicate that UTI localized in amnion is important in the protection of fetal membrane esp. against bacterial infections and cytokines. UTI inhibited uterine contractions stimulated by ET, PGF2.alpha., and oxytocin in the isometric contraction test. UTI could also inhibit cervical maturation induced by interleukin-8. Therefore, UTI is essential for maintenance of pregnancy. From the isometric contraction tests, the authors assumed that UTI might work through regulation of calcium entry or availability in the cells. Initial increase in intracellular calcium was also inhibited by UTI preincubation dose-dependently. The authors examd. the change in intracellular calcium at the single cell level by digital image anal. with fura 2 as a calcium probe. At the resting level, UTI incubation did not produce any changes in intracellular free Ca. Thrombin, LPS, interleukin-8 and ET-1, known calcium agonists, could increase intracellular Ca in fibroblasts, amnion, and uterine myocytes. The same doses of these calcium agonists could not change the intracellular free Ca concns. in UTI-preincubated fibroblasts, amnion cells, or uterine smooth muscle cells. Preincubation with **EGTA** inhibited the initial rise in intracellular Ca that reflects the Ca release from intracellular stores. On preincubation with UTI, the initial rise in intracellular Ca was also inhibited. These results agreed with the result of inhibition of myometrial contraction by UTI preincubation in isometric contraction tests. An inhibitory effect of UTI on calcium mobilization and entry was suggested by this study. Increased

intracellular free Ca also functions as a second messenger that dets. the cellular synthetic activities in many cells. With the idea that UTI inhibits the synthetic activities in cells, the authors examd. the effect of UTI preincubation on prodn. of interleukin-8, collagenase, and prostaglandin from amniotic cells and fibroblasts. LPS stimulated amnion cells and fibroblasts in culture and increased prodn. of interleukin-8, collagenase and prostaglandin. Preincubation with UTI depressed the prodn. of interleukin-8, collagenase, and prostaglandin from the amnion cells and fibroblasts. Preincubation with UTI also attenuated the increase in the appearance of interleukin-8 mRNA in LPS-stimulated amnion and fibroblasts. From these series of expts. the authors concluded that UTI regulates the prodn. of inflammatory mediators by controlling intracellular free Ca2+. Treatment of mild cases of imminent preterm delivery with UTI suppositories significantly lowered preterm birth rate.

L15 ANSWER 7 OF 11 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:574551 HCAPLUS
DOCUMENT NUMBER: 121:174551
TITLE: Stability of albumin, protein HC, immunoglobulin G, .kappa. and .lambda.-chain immunoreactivity, orosomucoid and .alpha.1-**antitrypsin** in **urine** stored at various conditions
AUTHOR(S): Tencer, J.; Thysell, H.; Andersson, K.; Grubb, A.
CORPORATE SOURCE: Dep. Nephrol., Lund Univ. Hosp., Lund, S-221 85, Swed.
SOURCE: Scandinavian Journal of Clinical and Laboratory Investigation (1994), 54(3), 199-206
CODEN: SJCLAY; ISSN: 0036-5513
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Urine samples from 10 randomly selected patients with advanced renal disease were each divided into six aliquots and a preservative soln. contg. benzamidinium chloride, **EDTA**, tris(hydroxymethyl)-aminomethane and azide was then added to three of the aliquots. Aliquots with and without additive were then stored at room temp. for up to 7 days, at 4.degree.C for up to 30 days and at -20.degree.C for up to 6 mo.
IT **60-00-4**, **EDTA**, uses
RL: USES (Uses)
(in study of stability of albumin, protein HC, IgG, .kappa. and .lambda.-chain immunoreactivity, orosomucoid and .alpha.1-**antitrypsin** in **urine**)

L15 ANSWER 8 OF 11 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:238789 HCAPLUS
DOCUMENT NUMBER: 120:238789
TITLE: Two forms of acidic arginine amidases in human kidney
AUTHOR(S): Ishikawa, Hiromichi; Matsuda, Yoshifumi; Kaneko, Satoru; Yazaki, Tunetada; Umeda, Takasi; Fujimoto, Yukio; Akihama, Sumiyuki
CORPORATE SOURCE: Dep. Urol., Ichikawa Gen. Hosp., Chiba, Japan
SOURCE: Japanese Journal of Nephrology (1993), 35(11), 1277-82
CODEN: NJGKAU; ISSN: 0385-2385
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two forms of acidic arginine amidases were sepd. from human kidney ext. using the techniques of basic ion-exchange adsorption and elution as well as lima bean trypsin inhibitor (LBTI) and aprotinin affinity adsorptions and elutions. The enzymes were tentatively named acidic human renal arginine amidase-L (AHRAA-L, with affinity to an LBTI column) and -A

(AHRAA-A, with affinity to an aprotinin column). Both enzymes showed a similar mol. mass of .apprx.3.0 .times. 104 Da, differing from that of human renal kallikrein (HRK, mol. mass of 4.8 .times. 104 Da). The specific activity of AHRAA-L and -A were 106 and 680 nmol/min/A280 of Val-Leu-Arg-pNA amidolysis, resp., and they were strongly inhibited by LBTI and human **urinary trypsin** inhibitor (UTI), while **EGTA** showed a weak or no effect on both enzymes.

L15 ANSWER 9 OF 11 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:250861 HCAPLUS
DOCUMENT NUMBER: 116:250861
TITLE: Endopeptidase and carboxypeptidase activities in human urine which hydrolyze bradykinin
AUTHOR(S): Casarini, D. E.; Alves, K. B.; Araujo, M. S.; Stella, R. C. R.
CORPORATE SOURCE: Dep. Bioquim., Esc. Paulista Med., Sao Paulo, 04044, Brazil
SOURCE: Brazilian Journal of Medical and Biological Research (1992), 25(3), 219-29
CODEN: BJMRDK; ISSN: 0100-879X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The bradykinin-inactivating activity of human urine was fractionated by stepwise elution chromatog. on DEAE-cellulose and 95% of the inactivating activity and 29% of the protein (absorbance at A280 nm) was recovered. Seven of nine fractions which presented activity were also tested for angiotensin I and II inactivating activity, angiotensin converting activity and for the hydrolysis of hippuryl-His-Leu and hippuryl-Arg. Sites of hydrolysis in bradykinin were detd. by HPLC of the hydrolyzates and fragments were compared with authentic peptides. Cleavage sites demonstrated for Fractions A through G were: Phe8-Arg9 (A and B), Phe5-Ser6 (C and F), Pro7-Phe8 (D), Gly4-Phe5 and Pro7-Phe8 (E) and Pro3-Gly4 (G). The relative mol. wt. of the bradykininase activity present in each fraction, detd. by gel filtration, was: 16 kDa (A), 70 kDa (B), 60 kDa (C), 88 kDa (D), 230 kDa (E), 45 kDa (F) and 49 kDa (G). Bradykinin-inactivating activity was inhibited 50-100% by 3 mM **EDTA** (A, B, D, E and G), 1 mMM 2-mercaptoethanol (A, B, C and G), 0.1 .mu.M Hg2+ (A, C and G), 0.1 mM PMSF (C and F), 1 mM TPCK (C and F), 1 mM Zn2+ (C), 60 .mu.M BPP5a and 40 .mu.M BPP9a (D), 0.1 .mu.M phosphoramidon (E) and 3 mM sodium p-hydroxymercuribenzoate (G). The properties of some of these bradykinin-inactivating activities correspond to enzymes previously described in urine and tissues: carboxypeptidases (Fractions A and B), angiotensin I-converting enzyme (Fraction D), neutral endopeptidase (Fraction E). However, the chymotrypsin-like activity of Fractions C and F and the polyendopeptidase activity of Fraction G have not been described in urine.

L15 ANSWER 10 OF 11 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1986:104810 HCAPLUS
DOCUMENT NUMBER: 104:104810
TITLE: Studies on fibrinolytic enzyme in human bronchoalveolar lavage fluid
AUTHOR(S): Takagi, Ohmi
CORPORATE SOURCE: Sch. Med., Kinki Univ., Osaka, Japan
SOURCE: Kinki Daigaku Igaku Zasshi (1985), 10(3), 221-37
CODEN: KDIZDD; ISSN: 0385-8367
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

AB A fibrinolytic enzyme from the sol. fraction of human bronchoalveolar lavage fluid (BALF) was characterized. SDS-polyacrylamide gel electrophoresis and enzymog. of the fibrinolytic enzyme revealed that its mol. wt. was 58,000. From the enzymic activity interaction with diisopropyl fluophosphate, this enzyme was thought to be a serine proteinase. Enzymic activity was inhibited by dithiothreitol, 2-mercaptoethanol, aprotinin, soybean **trypsin** inhibitor, and **urinary trypsin** inhibitor, but not inhibited by benzamidine, **EDTA**, Na p-tosyl-L-lysine chloromethyl ketone, tosylamide-2-phenylethyl chloromethyl ketone, amino-n-caproic acid, pepstatin, chymostatin and antipain. However, this enzyme was adsorbed on a fibrin-Sepharose, showing no fibrin affinity. In amidolytic activity with synthetic substrates S-2444 and S-2288, enhancement in absorbance due to the reaction with S-2288 was assumed to be the same reaction to tissue plasminogen activator (TPA). When reacted with urokinase (UK) IgG antibody, it lost enzymic activity, but showed no reaction with an antibody to TPA.

L15 ANSWER 11 OF 11 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1983:49432 HCAPLUS
DOCUMENT NUMBER: 98:49432
TITLE: Isolation of a human **urinary trypsin** inhibitor
AUTHOR(S): Balduyck, M.; Hayem, A.; Kerckaert, J. P.; Mizon, C.; Mizon, J.
CORPORATE SOURCE: Lab. Biochim., Fac. Pharm., Lille, 59045, Fr.
SOURCE: Biochemical and Biophysical Research Communications (1982), 109(4), 1247-55
CODEN: BBRCA9; ISSN: 0006-291X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Stabilization of the **antitrypsin** activity of human **urine** was obtained by storage at neutral pH in the presence of **EDTA** and a **urinary trypsin** inhibitor was isolated in a pure state and partially characterized.

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=> d que stat l17
L1             1 SEA FILE=REGISTRY ABB=ON  EGTA/CN
L2             1 SEA FILE=REGISTRY ABB=ON  EDTA/CN
L3             1 SEA FILE=REGISTRY ABB=ON  "NITRILOTRIACETIC ACID"/CN
L4             1 SEA FILE=REGISTRY ABB=ON  "IMINODIACETIC ACID"/CN
L5             1 SEA FILE=REGISTRY ABB=ON  DTPA/CN
L6             1 SEA FILE=REGISTRY ABB=ON  TTHA/CN
L7             1 SEA FILE=REGISTRY ABB=ON  "PROPYLENEDIAMINETETRAACETIC
                 ACID"/CN
L8             1 SEA FILE=REGISTRY ABB=ON  "1,2-DIAMINOCYCLOHEXANETETRAACETIC
                 ACID"/CN
L9             8 SEA FILE=REGISTRY ABB=ON  L1 OR L2 OR L3 OR L4 OR L5 OR L6 OR
                 L7 OR L8
L10       101593 SEA FILE=HCAPLUS ABB=ON  L9 OR ?EGTA? OR ?EDTA? OR ?DTPA? OR
                 ?TTHA?
L11         7995 SEA FILE=HCAPLUS ABB=ON  (?IMINODIACETIC? OR ?IMINO?(W)?DIACETI
                 C? OR ?NITRILOTRIACETIC? OR ?NITRILO(W)TRIACETIC? OR ?PROPYLENE
                 DIAMINOTETRAACETIC? OR ?PROPYLENEDIAMINO(W)TETRA(W)ACETIC? OR
                 ?DIAMINOCYCLOHEXANETETRAACETIC? OR ?DIAMINO(W)CYCLOHEXANE(W)TET
                 RA(W)ACETIC?)(W)?ACID?
L12       104964 SEA FILE=HCAPLUS ABB=ON  L10 OR L11
L15           11 SEA FILE=HCAPLUS ABB=ON  L12 AND URIN?(3A)(?TRYPSIN? OR
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?TRYPSIN(3A)SUBSTRATE?)
L16 17 SEA L15
L17 9 DUP REMOV L16 (8 DUPLICATES REMOVED)

L17 ANSWER 1 OF 9 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-107797 [15] WPIDS
DOC. NO. CPI: C2002-033267
TITLE: A new assay for **trypsin** inhibitors in **urine** by contacting the **urine** with **trypsin** and a **substrate** which gives a detectable cleavage product can be prepared as a dry phase assay and is useful to detect kidney diseases.
DERWENT CLASS: B04 D16
INVENTOR(S): COREY, P F; PUGIA, M J; REHM, G E; REHM, G B
PATENT ASSIGNEE(S): (FARB) BAYER CORP; (MILE) MILES LAB INC; (CORE-I) COREY P F; (PUGI-I) PUGIA M J; (REHM-I) REHM G E
COUNTRY COUNT: 33
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 1156121	A2	20011121	(200215)*	EN	5
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR					
CA 2334321	A1	20011115	(200215)	EN	
NO 2001002262	A	20011116	(200215)		
US 2001055816	A1	20011227	(200215)		
ZA 2001002449	A	20011128	(200215)		26
JP 2002014096	A	20020118	(200221)		8
AU 2001026506	A	20020725	(200260)		
NZ 509904	A	20020830	(200265)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
EP 1156121	A2		EP 2001-110137	20010504
CA 2334321	A1		CA 2001-2334321	20010206
NO 2001002262	A		NO 2001-2262	20010508
US 2001055816	A1	Provisional	US 2000-204032P	20000515
			US 2001-844815	20010430
ZA 2001002449	A		ZA 2001-2449	20010326
JP 2002014096	A		JP 2001-142654	20010514
AU 2001026506	A		AU 2001-26506	20010313
NZ 509904	A		NZ 2001-509904	20010213

PRIORITY APPLN. INFO: US 2000-204032P 20000515; US 2001-844815 20010430
AN 2002-107797 [15] WPIDS
AB EP 1156121 A UPAB: 20020306
NOVELTY - A new assay (M1) for **trypsin** inhibitors in **urine** comprises contacting test urine with a medium containing trypsin, a trypsin substrate which produces a detectable response when cleaved by trypsin, and a polycarboxylic chelating agent sufficient to inhibit calcium interference, and correlating the detectable response with the concentration of trypsin inhibitor.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is included for a method

(M2) preparing a test device for determination of a **trypsin** inhibitor in **urine**, comprising contacting a pad of absorbent material with an aqueous solution of trypsin and poly carboxylic chelating agent followed by drying the strip and contacting it with a solvent solution of a trypsin substrate with subsequent drying.

USE - The invention is used to assay for **trypsin** inhibitor in **urine**, which is a marker of kidney disease.

ADVANTAGE - Unlike prior art the assay of the invention is suitable as a dry phase assay.

Dwg.0/0

L17 ANSWER 2 OF 9 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1999-349236 [30] WPIDS
DOC. NO. CPI: C1999-103048
TITLE: Stabilizing trypsin and/or increasing trypsin enzymatic activity for use in food industry, detergents, biochemical and/or clinical tests.
DERWENT CLASS: B04 D13 D16 D25 E19 E37
INVENTOR(S): YONEHARA, S
PATENT ASSIGNEE(S): (KYOT-N) KYOTO DAIICHI KAGAKU CO LTD; (KYOT-N) KYOTO DAIICHI KAGAKU KK; (ARKR-N) ARKRAY INC
COUNTRY COUNT: 27
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 926235	A2	19990630	(199930)*	EN	14
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
JP 11164699	A	19990622	(199935)		12
US 6177268	B1	20010123	(200107)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 926235	A2	EP 1998-309920	19981203
JP 11164699	A	JP 1997-336160	19971205
US 6177268	B1	US 1998-203195	19981130

PRIORITY APPLN. INFO: JP 1997-336160 19971205
AN 1999-349236 [30] WPIDS
AB EP 926235 A UPAB: 19990802

NOVELTY - The method for stabilizing trypsin and/or increasing enzymatic activity of trypsin comprises, dissolving trypsin in a buffer solution having a pH at which trypsin is active and containing calcium and/or manganese ions to form a stabilized trypsin solution.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a method for measuring enzymatic activity of trypsin comprising:

(a) dissolving trypsin in a buffer solution having a pH at which trypsin is active and containing calcium and/or manganese ions to form a stabilized trypsin solution; and

(b) adding a substrate for trypsin to the stabilized trypsin solution;

(2) a kit for measuring enzymatic activity of trypsin, comprising a stabilized trypsin solution (as above);

(3) a stabilized trypsin solution (as above); and

(4) a method for the preparation of a reagent for use in measuring the enzymatic activity of trypsin comprising drying the above solution.

USE - The stabilized trypsin solution is useful in a field where the generation of enzyme reaction of trypsin is required e.g. food industry, detergents, tests for clinical medicine and biochemistry and for measuring **urinary trypsin** inhibitor (UTI) etc.

ADVANTAGE - The method has improved test precision, processing speed and improved efficiency.

Dwg.0/0

L17 ANSWER 3 OF 9 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 97213322 MEDLINE
DOCUMENT NUMBER: 97213322 PubMed ID: 9060087
TITLE: Long-term stability of albumin, protein HC, immunoglobulin G, kappa- and lambda-chain-immunoreactivity, orosomucoid and alpha 1-**antitrypsin** in **urine** stored at -20 degrees C.
AUTHOR: Tencer J; Thysell H; Andersson K; Grubb A
CORPORATE SOURCE: Department of Nephrology, Lund University Hospital, Sweden.
SOURCE: SCANDINAVIAN JOURNAL OF UROLOGY AND NEPHROLOGY, (1997 Feb) 31 (1) 67-71.
Journal code: 0114501. ISSN: 0036-5599.
PUB. COUNTRY: Sweden
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970612
Last Updated on STN: 19970612
Entered Medline: 19970530

AB The stability of albumin, protein HC, immunoglobulin G, kappa- and lambda-chain immunoreactivity, orosomucoid and alpha 1-**antitrypsin** in **urine** stored at -20 degrees C for up to 24 months was investigated. Significant decreases of the median concentration values for protein HC, IgG and alpha 1-antitrypsin were observed for native urine. Addition to urine of a preservative solution containing benzamidinium chloride, **EDTA**, tris(hydroxymethyl)-aminomethane and azide prevented the decreases of the concentration values for protein HC and IgG but not for alpha 1-antitrypsin. The median concentration values for albumin, orosomucoid and kappa- and lambda-chain immunoreactivity did not change significantly upon storage of native urine, nor for urine with the preservative solution.

L17 ANSWER 4 OF 9 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 95160693 MEDLINE
DOCUMENT NUMBER: 95160693 PubMed ID: 7857284
TITLE: Kunitz-type trypsin inhibitor prevents LPS-induced increase of cytosolic free Ca2+ in human neutrophils and HUVEC cells.
AUTHOR: Kanayama N; Halim A; Maehara K; Kajiwara Y; Fujie M; Terao T
CORPORATE SOURCE: Department of Obstetrics and Gynecology, Hamamatsu University School of Medicine, Japan.
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1995 Feb 6) 207 (1) 324-30.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199503
ENTRY DATE: Entered STN: 19950322
Last Updated on STN: 19950322
Entered Medline: 19950314

AB The protease inhibitor part of inter-alpha trypsin inhibitor is identical to **urinary trypsin** inhibitor (UTI). Preincubation of neutrophils and HUVEC cells with UTI inhibited increase of cytosolic free Ca2+ induced by LPS. Increase of cytosolic free Ca2+ induced by LPS in the presence of **EGTA** was also inhibited by UTI. In contrast, UTI did not inhibit increase of cytosolic free Ca2+ in cells stimulated by Ca2+ ionophore with or without **EGTA**. The effects of nine synthetic peptides of UTI on the concentration of cytosolic free Ca2+ in the neutrophils induced by LPS were examined. Preincubation with a peptide of UTI domain 2, NLPIVRGPCRAFIQL (83-97), was completely inhibited by the increase of cytosolic free Ca2+ in neutrophils. This region is identical to the trypsin inhibitor site of UTI. We propose that a function of UTI other than as a protease inhibitor is in regulation of intracellular Ca2+ and that this is due to its trypsin inhibitor region.

L17 ANSWER 5 OF 9 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 94278496 EMBASE
DOCUMENT NUMBER: 1994278496
TITLE: Intrauterine defensive mechanism of amniotic fluid and fetal membranes.
AUTHOR: Kanayama N.
CORPORATE SOURCE: Department of Obstetrics/Gynecology, Hamamatsu Univ. School of Medicine,Hamamatsu, Japan
SOURCE: Acta Obstetrica et Gynaecologica Japonica, (1994) 46/8 (673-685).
ISSN: 0300-9165 CODEN: AOGLAR
COUNTRY: Japan
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 010 Obstetrics and Gynecology
029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: Japanese
SUMMARY LANGUAGE: English

AB To determine the intrauterine defensive role of **urinary trypsin** inhibitor (UTI), we studied the effects of UTI in amniotic fluid, fetal membranes and myometrium. The level of UTI was 94 .+-. 34 U/ml in neonatal urine (compared to adult urine 8.0 .+-. 6.0 U/ml) and 88 .+-. 37 U/ml in amniotic fluid. This may indicate that the main source of UTI in the amniotic fluid is the fetal urine. UTI was found to be concentrated in vernix, fetal intestine, amniotic membranes and uterine myometrium. Immunostaining of term amnion revealed a dark staining for UTI, whereas in premature deliveries UTI staining was markedly decreased. In myometrium, the concentration of UTI was found to be increased during pregnancy compared to non pregnant myometrium. Also, placentas were well stained for UTI in term pregnancy. Thus UTI has an important role in amniotic fluid, fetal membranes, placenta and uterine muscles. UTI has an inhibitory effect on several enzymes and cytokines. UTI was found to inhibit neutrophil elastase activity as well as trypsin activity. Its inhibitory activity was increased in the presence of lipid. LPS stimulated amnion cells trapped more UTI than unstimulated amnion cells. UTI in amnion cells was released after addition of 1% meconium solution. UTI was

also found to inhibit the effect of IL-1, TNF and interleukin-8 on amnion. These results indicate that UTI localized in amnion is important in the protection of fetal membrane especially against bacterial infections and cytokines. It is known that endothelin (ET), prostaglandin F(2.alpha.) (PGF(2.alpha.)) and oxytocin can induce uterine contraction. UTI could inhibit uterine contractions stimulated by ET, PGF(2.alpha.) and oxytocin in isometric contraction test. UTI could also inhibit cervical maturation induced by interleukin-8. Therefore UTI is essential for maintenance of pregnancy. From the isometric contraction tests, we assumed that UTI might work through regulation of calcium entry or availability in the cells. Initial increase in intracellular calcium was also inhibited by UTI pre incubation dose dependantly. We examined the change in intracellular calcium at single cell level by digital image analysis with Fura 2AM as a calcium probe. At resting level UTI incubation did not produce any significant changes in intracellular free calcium. Thrombin, LPS, interleukin-8 and ET-1, known calcium agonists could increase intracellular calcium in fibroblasts, amnion and uterine myocytes. Whereas as the same doses of those known calcium agonists could not change the intracellular free Ca2+ concentrations in UTI pre incubated fibroblasts, amnion cells and uterine smooth muscle cells. Pre incubation with 2nM **EGTA** could inhibit the initial rise in intracellular calcium that reflects the calcium release from intracellular stores. However pre incubation with UTI, the initial rise in intracellular calcium was also inhibited. These results agreed the result of inhibition of myometrial contraction by UTI pre incubation in isometric contraction tests. The inhibitory effect of UTI on calcium mobilization and entry was suggested by this study. Increased intracellular free calcium also functions as a second messenger that determines the cellular synthetic activities in many cells. With the idea that UTI inhibits the synthetic activities in cells, we examined the effect of UTI pre incubation on production of interleukin-8, collagenase and prostaglandin from the amniotic cells and fibroblasts. LPS stimulated amnion cells and the fibroblast cultures and significantly increased production of interleukin-8, collagenase and prostaglandin from them. Whereas as pre incubation with UTI, the production of interleukin-8, collagenase and prostaglandin from the amnion cells and fibroblasts was depressed. LPS could increase significantly the appearance of mRNA of interleukin-8 in amnion and fibroblast cells. We also examined the effect of UTI pre incubation on the appearance of mRNA in LPS stimulated cells. The appearance of mRNA of interleukin-8 in those cells was inhibited in the presence of UTI. From these series of experiments, we concluded that UTI regulates the production of inflammatory mediators by the control of intracellular free Ca2+: a second messenger.

L17 ANSWER 6 OF 9 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 94310382 MEDLINE
DOCUMENT NUMBER: 94310382 PubMed ID: 7518610
TITLE: Stability of albumin, protein HC, immunoglobulin G, kappa- and lambda-chain immunoreactivity, orosomucoid and alpha 1-**antitrypsin** in **urine** stored at various conditions.
AUTHOR: Tencer J; Thysell H; Andersson K; Grubb A
CORPORATE SOURCE: Department of Nephrology, Lund University Hospital, Sweden.
SOURCE: SCANDINAVIAN JOURNAL OF CLINICAL AND LABORATORY INVESTIGATION, (1994 May) 54 (3) 199-206.
Journal code: 0404375. ISSN: 0036-5513.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199408
ENTRY DATE: Entered STN: 19940825
Last Updated on STN: 19960129
Entered Medline: 19940816

AB Urine samples from 10 randomly selected patients with advanced renal disease were each divided into six aliquots and a preservative solution containing benzamidinium chloride, EDTA, tris(hydroxymethyl)-aminomethane and azide was then added to three of the aliquots. Aliquots with and without additive were then stored at room temperature for up to 7 days, at 4 degrees C for up to 30 days and at -20 degrees C for up to 6 months. The concentrations of albumin, protein HC, IgG, orosomucoid and alpha 1-antitrypsin as well as the kappa- and lambda-chain immunoreactivities in the samples were determined by automated immunoturbidimetry or by single radial immunodiffusion after 1, 3, 7, 14, 30, 90 and 180 days of storage. All investigated proteins, except alpha 1-**antitrypsin** in native **urine**, were stable for 7 days in the samples stored at room temperature both in the presence and absence of additives. All investigated proteins, except alpha 1-**antitrypsin** in native **urine**, were stable for 30 days in the samples stored at 4 degrees C both in the presence and absence of additives. A more complex pattern was observed for the stability of the proteins in the frozen samples. The IgG level decreased rapidly in several samples stored without additives but not in samples stored with additives. The alpha 1-antitrypsin concentration decreased rapidly to about 50% of the initial value in several samples stored both with and without additives. The rate of the decrease for both the IgG and the alpha 1-antitrypsin level varied between samples and the main decrease for several samples was seemingly caused by the freezing and/or thawing per se and not by the storage period in between.

L17 ANSWER 7 OF 9 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1993-061643 [08] WPIDS
DOC. NO. CPI: C1993-027794
TITLE: Human **urine** derived **trypsin** inhibitor prepn., in high yield - prepd. by treating aq. soln. of human **urine** derived **trypsin** inhibitor with metal chelate resin and/or hydrophobic carrier.
DERWENT CLASS: B04
PATENT ASSIGNEE(S): (GREC) GREEN CROSS CORP
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
JP 05009200	A	19930119	(199308)*		8
JP 2722140	B2	19980304	(199814)		7

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
JP 05009200	A	JP 1991-161828	19910702
JP 2722140	B2	JP 1991-161828	19910702

FILING DETAILS:

PATENT NO	KIND	PATENT NO
JP 2722140	B2 Previous Publ.	JP 05009200

PRIORITY APPLN. INFO: JP 1991-161828 19910702
AN 1993-061643 [08] WPIDS
AB JP 05009200 A UPAB: 19931119
Inhibitor is prepd. by treating human **urine** derived **trypsin** inhibitor-contg. aq. soln. with metal chelate resin and/or hydrophobic carrier.

USE/ADVANTAGE - Highly purified inhibitor is obtd. in good yield.

In an example, starting material was prepd., from human urine, according to J.P.O. Sho. 62-93238. pH of the starting material (420ml) was adjusted to 6.4, and applied to QAE-agarose gel equilibrated with 0.1M phosphate buffer (pH 6.4), next, eluted with 0.5M NaCl added 0.1M phosphate buffer (pH 6.4) to recover the inhibitor-contg. fraction. pH of eluted fraction (400ml) was adjusted to 7.9, and applied to Cu(2+) chelate agarose gel equilibrated with 0.5M NaCl added 0.1M phosphate buffer to recover non-adsorbed fraction. To this (840 ml), 2M (NH4)2SO4 was added to regulate concn. to 0.8M, and applied to phenyl-agarose gel equilibrated with 0.8M (NH4)2SO4 added 6 mM phosphate buffer (pH 6.0) to recover non-adsorbed fraction. To this (1520 ml), **EDTA** was added at 1 mM, and concn. by ultra filtration to recover concn. fraction. This (36 ml) was applied to polyacrylamide gel equilibrated with 0.3M NaCl added 0.1M phosphate buffer (pH 6.2), and objective fraction was recovered with the same buffer. m.wt. 67,000, specific activity 4922 units/OD280.
Dwg.0/0

L17 ANSWER 8 OF 9 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 94187222 MEDLINE
DOCUMENT NUMBER: 94187222 PubMed ID: 8139142
TITLE: Two forms of acidic arginine amidases in human kidney.
AUTHOR: Ishikawa H; Matsuda Y; Kaneko S; Yazaki T; Umeda T; Fujimoto Y; Akihama S
CORPORATE SOURCE: Department of Urology, Ichikawa General Hospital, Tokyo Dental College, Chiba, Japan.
SOURCE: NIPPON JINZO GAKKAI SHI. JAPANESE JOURNAL OF NEPHROLOGY, (1993 Nov) 35 (11) 1277-82.
Journal code: 7505731. ISSN: 0385-2385.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199404
ENTRY DATE: Entered STN: 19940509
Last Updated on STN: 19940509
Entered Medline: 19940428

AB Two forms of acidic arginine amidases were separated from human kidney extract using the techniques of basic ion exchange adsorption and elution as well as lima bean trypsin inhibitor (LBTI) and aprotinin affinity adsorptions and elutions. The enzymes were tentatively named acidic human renal arginine amidase-L (AHRAA-L, with affinity to an LBTI column) and -A (AHRAA-A, with affinity to an aprotinin column). Both enzymes showed a similar molecular mass of approximately 3.0 x 10(4) daltons, differing from that of human renal kallikrein (HRK, molecular mass of 4.8 x 10(4) daltons). The specific activity of AHRAA-L and -A were 106 and 680 nmol/min/A280 of Val-Leu-Arg-pNA amidolysis, respectively, and they were strongly inhibited by LBTI and human **urinary trypsin**

inhibitor (UTI), while ethylenglycol-bis(beta-amino ethylether)-N,N,N',N'-tetraacetic acid (**EGTA**) showed a weak or no effect on both enzymes.

L17 ANSWER 9 OF 9 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 83178082 MEDLINE
DOCUMENT NUMBER: 83178082 PubMed ID: 6820282
TITLE: Isolation of a human **urinary trypsin** inhibitor.
AUTHOR: Balduyck M; Hayem A; Kerckaert J P; Mizon C; Mizon J
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1982 Dec 31) 109 (4) 1247-55.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198305
ENTRY DATE: Entered STN: 19900318
Last Updated on STN: 19900318
Entered Medline: 19830505